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Nickel (0)-Catalyzed Diene-Aldehyde Cyclization

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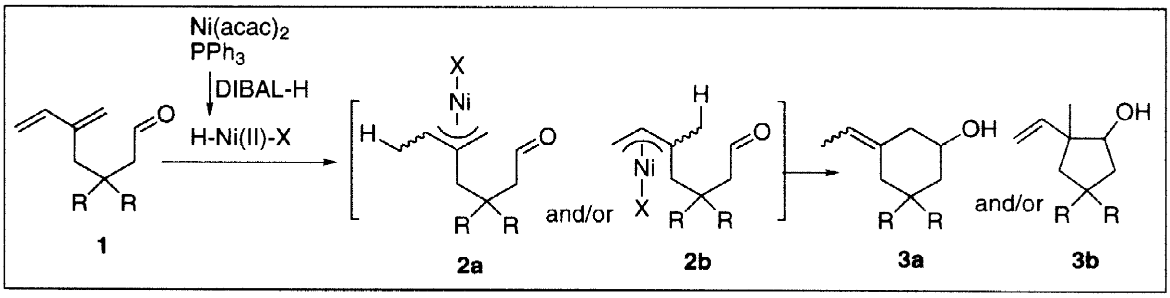
Abstract:

Nickel (0)-catalyzed diene-aldehyde cyclization was realized. In this reaction, oxidative cyclization between diene and aldehyde moiety occurs to give π-allylnickel complex, and then β-hydride elimination occurs to give cyclized diene. Various diene-aldehydes having substituents on the diene gave the cyclized products using Ni (0) in good to moderate yields. © 1998 Elsevier Science Ltd. All rights reserved.

Key Words: Ni(cod)$_2$; Nickel-catalyzed Cyclization; Diene; β-Hydride Elimination; Oxidative Cyclization.

Nickel-promoted cyclization between multiple bonds is quite interesting, and it is useful in synthetic organic chemistry.[1] We found the highly regio- and stereo-controlled diene-aldehyde cyclization[2] using hydridenickel complex (HNiX) generated from Ni(acac)$_2$ and DIBAl-H in the presence of PPh$_3$[3]. It is expected that when diene-aldehyde **1** having a tether at the 2-position of the diene moiety is treated with HNiX generated from Ni(acac)$_2$ and DIBAL-H in the presence of PPh$_3$, π-allyl nickel complex **2a** or **2b** is formed, and a new carbon-carbon bond is formed to produce cyclized product **3a** or **3b**. Our plan is shown in Scheme 1.

Scheme 1. Our Plan for Nickel-Promoted Diene-Aldehyde Cyclization



A THF solution of **1a** (1 equiv.) was added to a THF solution of nickel catalyst prepared from Ni(acac)$_2$ (1 equiv.), PPh$_3$ (2 equiv.) and DIBAL-H (2 equiv.), and the solution was stirred at 0 °C for 1.5 h. After hydrolysis of the reaction mixture, we obtained cyclized product **4a** in 13% yield along with **5a** and **6a** in 15% and 11% yields,

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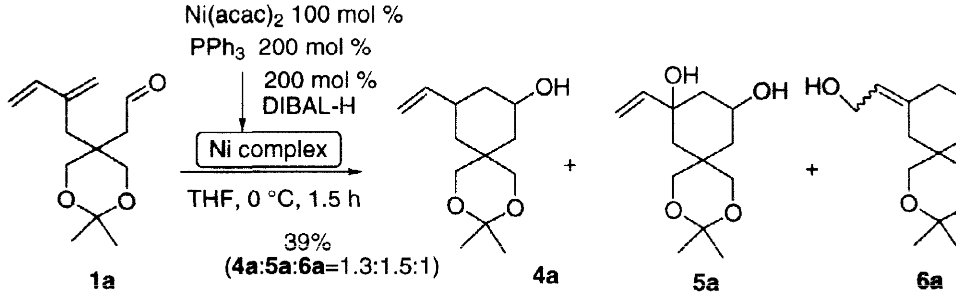
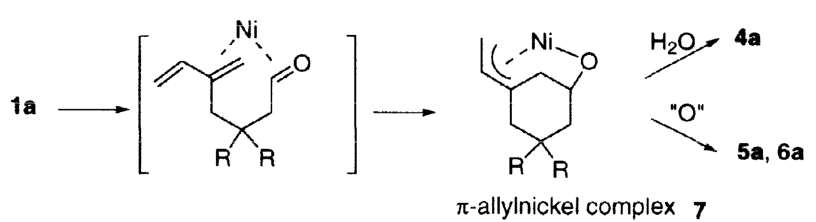
respectively. The formation of these products, especially the diols, **5a** and **6a**, could not be explained by our previous mechanism.[2a] Although various attempts were made to increase the yield of these compounds and to clarify the reaction mechanism (that is: the reaction mixture was treated with D_2O or oxygen, and the reaction was carried out under oxygen and at a low temperature (-30 to -50°C)), all attempts were fruitless.

If this reaction proceeds by Ni(0) complex, not HNiX, generated from $Ni(acac)_2$ and DIBAL-H in the presence of PPh_3 (Eq. 1),[3] oxidative cyclization would occur between diene and aldehyde moiety to produce π-allylnickel complex **7**. Hydrolysis of **7** would afford alcohol **4a**. Formation of **5a** and **6a** would be also explained by the reaction of **7** with oxygen, although the oxygen source is not clear. To confirm this assumption, the reaction was carried out using Ni(0).

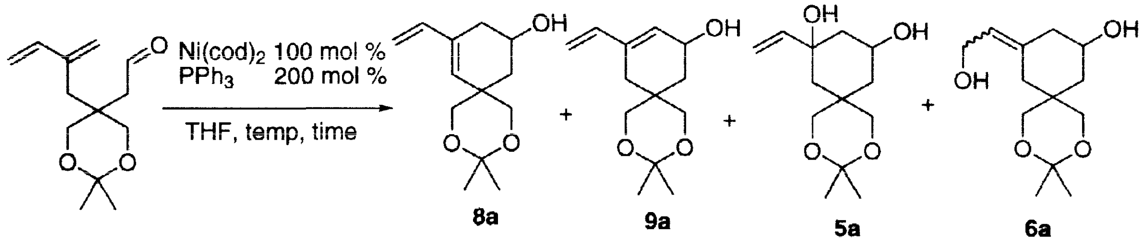


Scheme 2

$$\mathrm{Ni(acac)_2} \xrightarrow{\text{DIBAL-H}} \left[\,\text{H-Ni(II)-X}\,\right] \xrightarrow{\text{DIBAL-H}} \boxed{\text{Ni(0)}} \qquad \text{(eq. 1)}$$



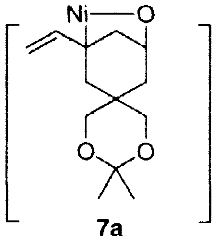
Scheme 3



Scheme 4

Table 1. Reaction of **1a** with $Ni(cod)_2$ and PPh_3

run	Temp (°C)	Time (h)	Total Yield (%)	yield (%) 8a+ 9a	ratio of 8a : 9a	yield (%) 5a + 6a
1	0	5	71	48	1 : 1.4	23
2	rt	5	76	64	1 : 3.2	12
3	rt	18	83	74	1 : 2.7	9
4	50	1	77	65	1 : 1.5	11

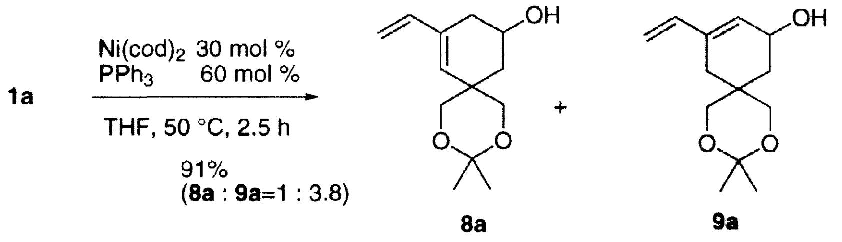


7a

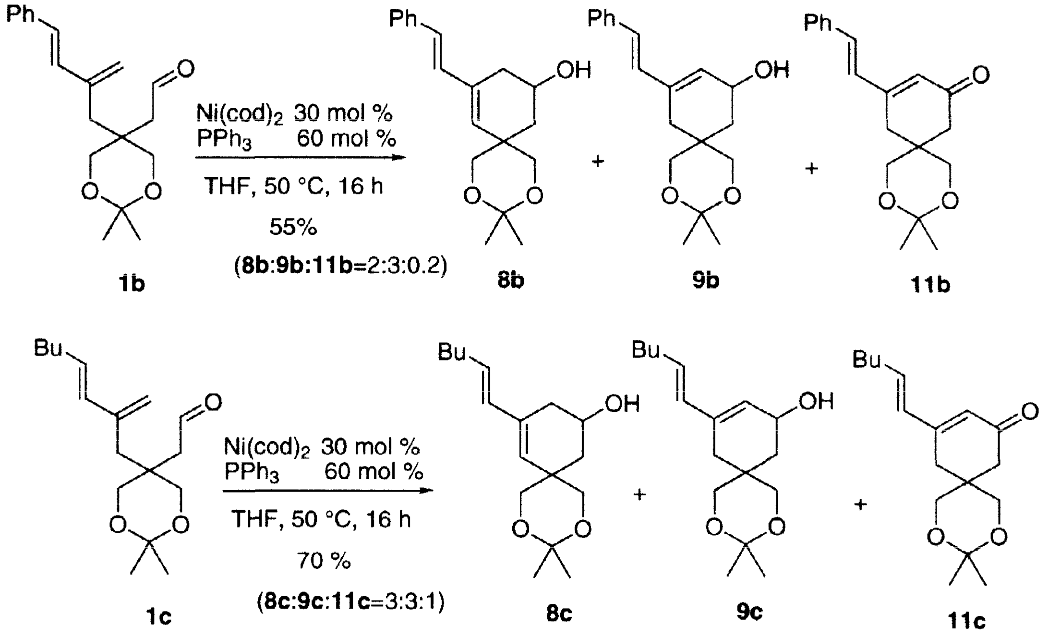
When a THF solution of **1a** (1 equiv.) was added to a THF solution of Ni(cod)$_2$ (1 equiv.) and PPh$_3$ (2 equiv.) at 0 °C and the solution was stirred at the same temperature for 5 h, the same products, **5a** and **6a**, were obtained in 23 % yields (Table 1, run 1). Interestingly, the main products in this reaction are **8a** and **9a**, in 48% yields (ratio of 1 to 1.4), which must be produced by β-hydride elimination from **7a**. A higher reaction temperature and longer reaction time accelerated β-hydride elimination from **7a** (runs 2 and 3). The fact that the yields of alcohols **5a** and **6a** decreased with a higher reaction temperature indicates that π-allylnickel complex is fairly stable at a low temperature and β-hydride elimination would occur at a high temperature.

It was thought that β-hydride elimination from **7a** would afford oxo-hydride nickel complex **10**, which should give **8a** or **9a** by reductive elimination. Thus, Ni(0) should be regenerated in this reaction (See Scheme 7). We succeeded in obtaining the desired products **8a** and **9a** in 91 % yield (ratio of 1 to 3.8) when the reaction was carried out using 30 mol % of Ni(cod)$_2$ and PPh$_3$ (60 mol %). The use of 10 mol % of the catalyst gave the desired products in 83% yield (ratio of 1 to 5.6).[4,5]

Subsequently, reactions of various substrates having substituents on the diene moiety were investigated using 30 mol % of Ni(cod)$_2$ and PPh$_3$. In each case, the desired cyclized products were obtained in good to moderate yields (Scheme 6). A small amount of oxidation product **11**, which would be formed by β-hydride elimination from **10**, was obtained in each case.[6]

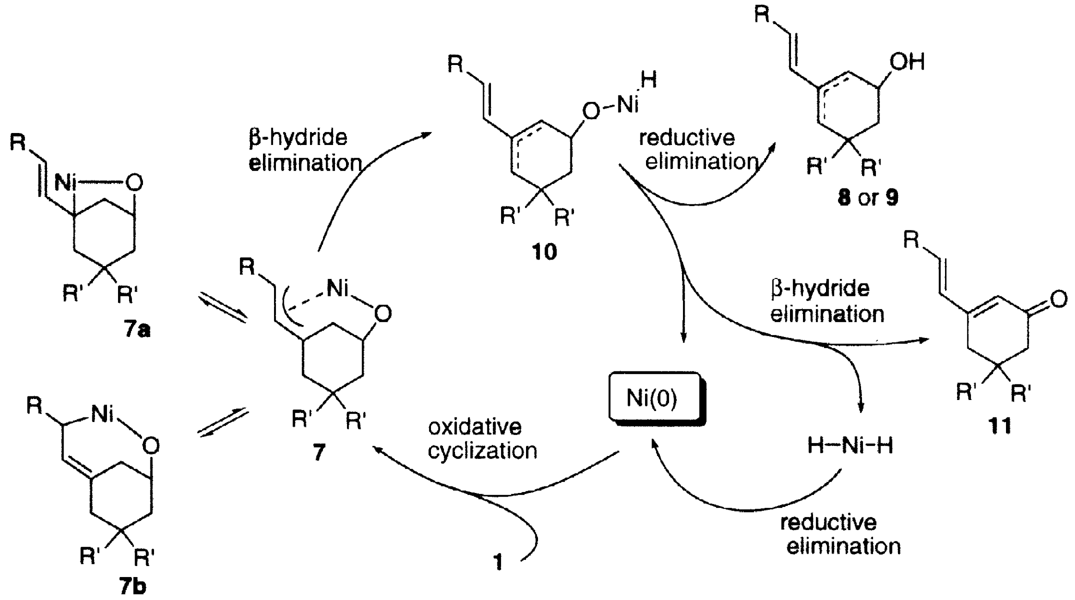


Scheme 5



Scheme 6

The probable reaction course is shown in Scheme 7. Oxidative cyclization occurs between diene and the aldehyde moiety of **1** to give π-allylnickel complex **7**, which is in a state of equilibrium with **7a** and **7b**. Then β-hydride elimination from **7a** occurs to give oxo-hydridenickel complex **10**. Reductive elimination from **10** gives **8** or **9** and Ni(0). On the other hand, β-hydride elimination from oxo-hydridenickel complex **10** gives α,β,γ,δ-unsaturated ketone **11** and dihydride nickel complex. From this dihydride nickel complex, Ni(0) would be regenerated. Thus, the catalytic cycle would be established.



Scheme 7

Further studies on this reaction are in progress.

References and Notes

[1] a) For [4 + 4] cycloadditions, see: Wender, P. A.; Tebbe, M. J. *Synthesis* **1991**, 1089 and references cited therein. b) For [4 + 2] cycloadditions, see: Wender, P. A.; Smith, T. E. *Tetrahedron* **1998**, *54*, 1255 and references cited therein. c) Montgomery, J.; Oblinger, E.; Savchenko, A. V. *J. Am. Chem. Soc.* **1997**, *119*, 4911. d) For reviews, see: Jolly, P. W. In *Comprehensive Organometallic Chemistry*; Wilkinson, G.; Stone, F. G. A.; Abel, E. W., Eds.; Pergamon: New York, 1982; Vol. 8, p 613. Kein, W.; Behr, A; Roper, M. *ibid.* p 371. Heimback, P. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 975. Wilke, G. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 185. e) Tamao, K.; Kobayashi, K.; Ito, Y. *Synlett* **1992**, 539. Tamao, K.; Kobayashi, K.; Ito, Y. *J. Synth. Org. Chem. Jpn.* **1990**, 48, 381. f) Baker, R.; Crimmin, M. J. *J. Chem. Soc. Perkin I* **1979**, 1264 and references cited therein.

[2] (a) Sato, Y.; Takimoto, M.; Hayashi, K.; Katsuhara, T.; Takagi, K.; Mori, M. *J. Am. Chem. Soc.* **1994**, *116*, 9771. (b) Sato, Y.; Takimoto, M.; Mori, M. *Tetrahedron Lett.* **1996**, *37*, 887. (c) Sato, Y.; Takimoto, M.; Mori, M. *Synlett* **1997**, 734. (d) Sato, Y.; Saito, N.; Mori, M. *Tetrahedron Lett.* **1997**, *38*, 3931. (e) Sato, Y; Saito, N; Mori, M. *Tetrahedron* **1998**, *54*, 1153.

[3] Krysan, D. J.; Mackenzie, P. B. *J. Org. Chem.* **1990**, *55*, 4229. See also 1e.

[4] Under the similar conditions, various ligands can be used. ($MePh_2P$; 84%(**8a**:**9a**=1:2.0), Me_2PhP; 91% (2.1:1), dppe; 46%(1:1.4), dppb; 91% (4.0:1)) (30 mol % of Ni(0), Ni : PR_3=1 : 2, in the case of bidentate ligand, Ni : PR_3=1 : 1).

[5] Previously, we considered that the nickel-promoted cyclization proceeded by HNiX generated from $Ni(acac)_2$ and DIBAL in the presence of PPh_3, because the reaction did not proceed by $Ni(cod)_2$ and PPh_3 and it proceeded by $Ni(cod)_2$ and PPh_3 in the presence of Et_3SiH.[2a] Now we are reinvestigating the mechanism of nickel-promoted cyclization by $Ni(acac)_2$ and DIBAL-H in the presence of PPh_3.

[6] Each compound, **8b** or **9b**, was oxidized with PCC to give the corresponding ketone in 52% or 70% yield, respectively.